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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/510,907	05/16/2005	Thomas Hogberg	62276(45579)	7331

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EDWARDS ANGELL PALMER & DODGE LLP
P.O. BOX 55874
BOSTON, MA 02205

EXAMINER	
LOEWE, SUN JAE Y	
ART UNIT	PAPER NUMBER
1609	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/510,907	HOGBERG ET AL.	
	Examiner	Art Unit	
	Sun Jae Y. Loewe	1609	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 April 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19 and 36-54* is/are pending in the application.

4a) Of the above claim(s) *36-44* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-19 and 45-54* is/are rejected.

7)☒ Claim(s) *1-19,45-54* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *08 October 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

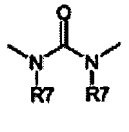
Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/16/2005*.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. *20070605*.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group I, and 2-Methoxy-4-[3-(3-phenoxy-phenyl)-ureido]-N-(3-piperidin-1-yl-propyl)-benzamide (Example 96, Interview Summary paper number 20070605), in the reply filed on April 24, 2007 is acknowledged. The restriction requirement mailed on March 9, 2007 is hereby made final.

2. Based on Applicant's election, the search and examination was performed for the core structure of claim 10 with the following limitations (see Scheme 1 on page 6): R^3 and R^4 joined to form a ring; Ar^1=Ar^2=phenyl; A=  ; B=  or  ; R^5 does not form ring; R^6 does not form ring.

The other variables (R^1, R^2, R^7, X, n) were allowed to assume the full scope of the definition provided in claim 1.

MPEP 1893.03(d) states that when all of the claims drawn to the elected invention are allowable (i.e., meet the requirements of 35 U.S.C. 101, 102, 103 and 112), the nonelected invention(s) should be considered for rejoinder. The instantly elected invention was not allowable under 35 U.S.C 112. Thus, the nonelected subject matter was *not* rejoined. The search and examination was performed *only* for the elected subject matter defined above.

3. Claims 36-44 withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected subject matter. Election was made **without** traverse in the reply filed on April 24, 2007.

Priority

4. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Information Disclosure Statement

5. The information disclosure statement (IDS) submitted on May 16, 2005 was in compliance with the provisions of 37 CFR 1.97 and 37 CFR 1.98. Accordingly, the information disclosure statement was considered. A signed copy of form PTO/SB/08a/b is submitted herewith.

Specification

6. This application does not contain a section for "Brief Description of Drawings" as required by 37 CFR 1.74. A section entitled "Brief Description of Drawings" is required.

Claim Objections

7. Claims 1-19, 45-54 objected to for containing non-elected subject matter.

8. Claim 1 objected to because of the following informalities: "alkoxy" is defined as a substituent twice for variables R^5 and R^6. Appropriate correction is required.

9. Claim 3 objected to because the term "cording" appears to be a typographical error and should read "according".

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

(Written Description)

10. Claims 1-19 and 45-54 rejected under 35 USC 112 1st paragraph as failing to comply with the written description requirement.

The MPEP states that the purpose of the written description requirement is to ensure that the inventor had possession, as of the filing date of the application, of the specific subject matter later claimed by him. The courts have stated:

> "To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997); In re Gostelli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966." Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.

Further, for a broad generic claim, the specification must provide adequate written description to identify the genus of the claim. In *Regents of the University of California v. Eli Lilly & Co.* the court stated:

> "A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *Fiers*, 984 F.2d at 1171, 25 USPQ2d 1601; *In re Smythe*, 480 F.2d 1376, 1383, 178 USPQ 279, 284985 (CCPA 1973) ("In other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus ...") *Regents of the University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398.

The MPEP states that for a generic claim the genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. MPEP § 2163. If the genus has a substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus. See MPEP § 2163. Although the MPEP does not define what constitute a sufficient number of representative species, the courts have indicated what do not constitute a representative number of species to adequately describe a broad genus. In *Gostelli*, the courts determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. *In re Gostelli*, 872, F.2d at 1012, 10 USPQ2d at 1618.

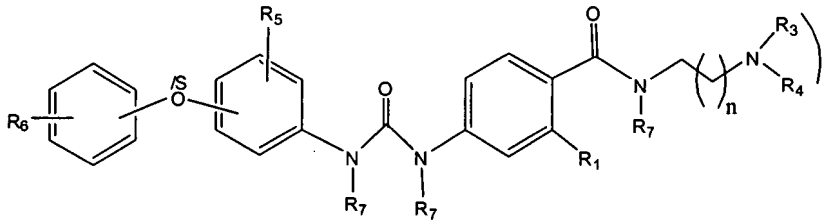
The Guidelines for Examination of Patent Applications Under 35 USC 112, ¶1, "Written Description" Requirement (Federal Register, Vol. 66, No. 4, pg. 1105, column 3), in accordance with MPEP § 2163, specifically states that for each claim drawn to a genus the written description requirement may be satisfied through sufficient description of a representative number of species by a) actual reduction to practice; b) reduction to drawings or structural chemical formulas; c) disclosure of relevant, identifying characteristics (ie. structure) by functional characteristics coupled with a known or disclosed correlation between function and structure. The analysis of whether the specification complies with the written description requirement calls for the examiner to compare the scope of the claim with the scope of the description to determine whether applicant has demonstrated possession of the claimed invention (Federal Register, Vol. 66, No. 4, p. 1105, 3rd column, 3rd paragraph). Below is such comparison.

I. *Scope of Claims* (based on ***elected*** subject matter)

(i) Claims 1-19 and 45-54: products with core structure defined in Scheme 1

- R^1, R^2, R^5-R^7 and X: scope of claims *congruent* with scope of disclosure
- R^3 and R^4: scope of claims *broad* relative to scope of disclosure

Scheme 1



(ii) Claim 17: amorphous or crystalline forms of the compounds in section (i)

(iii) Claim 19: solvates or prodrugs the compounds in section (i)

II. *Scope of Disclosure*

Reduction to Practice:

(i) Compounds reduced to practice support the following definitions for R^3 and R^4: joined together to form piperidine, piperazine, pyrrolidine or morpholine (all optionally substituted with alkyl or benzyl)

(ii)/(iii)No species reduced to practice

Reduction to Structural or Chemical Formulas:

(i) There is no disclosure of species in addition to those reduced to practice.

(ii) There is no disclosure of physical characteristics entailed by the genus encompassing "crystalline or amorphous" forms of the claimed compounds

(iii) There is no disclosure of physical characteristics for the genus encompassing "solvate" forms of the claimed compounds. There is no disclosure of structural or chemical formulas for prodrugs of the claimed compounds. There is no disclosure of any structural limitations specific to this genus of compounds that function as "prodrugs" of the claimed compounds.

Correlation between Structure and Function:

(i) A structure/activity relationship study has been shown for the instantly claimed genus of compounds as well as other compounds of similar structure (Receveur et al.). Although this study does not specifically address the effect of variables R^3 and R^4 to the activity of the claimed compounds, the following disclosure indicates that the activity does depend on the nature of these variables.

- Table 1 in p. 5078 of Receveur et al. show that morpholine substitution leads to a compound with approximately half the activity of piperidine substitution
- Receveur et al. further disclose (p. 5076, column 2, last paragraph), for a series of compounds which are structurally similar to the genus instantly claimed, that changes to the bulkiness of the alkyl group (ie. substituents that correspond to R^3 and R^4 in the instant compounds) results in noticeable changes in activity. Namely, substituting ethyl for methyl results in a 10-fold increase in activity.

In view of the absence of a correlation between structure and function for R^3 and R^4, one of ordinary skill would not expect that the entirety of the ring structures claimed for variables R^3 and R^4 would result in compounds with retained activity.

(ii) Correlation between structure and function is not applicable; ie. crystalline/amorphous forms of the claimed compounds are not defined or identified by functionality or chemical structure.

(iii) Correlation between structure and function is not applicable for the "solvates"; ie. solvates are not defined or identified by functionality or chemical structure. Prodrugs: absent any structural details, no correlation can be drawn between structure and function for the genus of compounds encompassed by the functional definition of "prodrugs".

III. *Analysis of Fulfillment of Written Description Requirement:*

(i) In summary: (a) substantial structural variation in the genus/subgenus embraced by the claims; (b) disclosure of species supporting genus is limited to compounds reduced to practice, which scope is not commensurate with the scope of genus claimed; (c) common structural attributes of the claimed genus, combined with a correlation between structure and function, is neither disclosed in the instant application nor commonly known in the art. Thus, the specification fails to provide adequate written description for the genus of compounds claimed and does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention.

(ii)/(iii)The description requirement of the patent statue requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See *In re Wilder*, 736, F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate.") Accordingly, it is deemed that the specification fails to provide adequate written description and does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

(Enablement)

12. Claims 1-19 and 45-54 rejected under 35 U.S.C. 112, first paragraph. The specification is enabling for the use of the compounds, within the claimed genus, that have adequate written description. The specification is not enabling for:

(a) how to use compounds, within the claimed genus, that are not supported by the disclosure

(b) how to make/use crystalline or amorphous forms of the claimed compounds

(c) how to make/use solvates or prodrugs of the claimed compounds

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The standard for determining whether the specification meets the enablement requirement was cast in the Supreme Court decision of *Mineral Separation v. Hyde*, 242 U.S. 261, 270 (1916) which postured the question: is the experimentation needed to practice the invention undue or unreasonable? That standard is still the one to be applied. *In re Wands*, 858 F.2d 731, 737, 8USPQ2s 1400, 1404 (Fed. Cir. 1988). MPEP 2164.01(a) states "There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is undue". The factors are applied below to the instant claims.

The breadth of the claims

(a) The claims are drawn to compounds with the structural limitations defined in section 10.

(b) The claims are drawn to crystalline or amorphous forms of the instantly claimed compounds.

(c) The claims are drawn to prodrugs or solvates of the instantly claimed compounds.

The nature of the invention

(i) The genus of compounds are disclosed to bind to and act as modulators of melanin concentrating hormone (MCH).

(ii)-(iii)The "invention" consists merely of a claim to crystalline/amorphous/solvate forms or prodrugs, for which there is no support in the specification.

The state of the prior art/level of ordinary skill/level of predictability

(i) The level of ordinary skill is high, but the level of predictability in the art is low, as discussed above in Section 10. Small changes to the nature of the core structure substitutions (eg. modification of variables R^3 and R^4 of Scheme 1) noticeably affects the binding of the compound to MCH, and therefore modulation activity. Thus, in the absence of guidance in the instant disclosure,

one of ordinary skill would not expect that the entirety of compounds embraced by the genus would possess the claimed activity. One of ordinary skill would not know which of the compounds not exemplified, if any, would possess the claimed activity.

(ii)-(iii)It is generally known that pharmaceuticals can exist in various solid forms – crystalline, amorphous, solvates - that have widely different physical and chemical properties (Chawla et al, p.9, 1st paragraph). The number of solid forms and properties cannot be predicted. In fact, the more diligently any system is studied the larger the number of solid forms discovered (Chawla et al., p. 9, 2nd column). Moreover, it is not predictable how different solid forms (including amorphous) are made (Newman et al., p. 898, 2nd column, last paragraph). Further, it is possible to have one solid form of an API be active while a different solid form is less active or altogether inactive (Chawla et al., p. 9, last paragraph).

(iii) Prodrug: the rationale behind the development of a prodrug is for optimization of absorption, distribution, metabolism, and excretion (http://en.wikipedia.org/wiki/Prodrug). Prodrug design can be classic (nonspecific chemical approach to mask undesirable properties) or targeted (strategic for selective delivery by targeting a specific enzyme or membrane transporter). See Han et al., p. 2 or 17. In either case, the design of a prodrug is an elaborate procedure involving a definition of purpose (eg. for better penetration of blood-brain barrier, http://en/wikipedia.org/wiki/Levodopa) and specific structural modification to obtain the desired therapeutic activity. Furthermore, biological data showing the efficacy of the prodrug for the targeted/desired purpose is necessary.

The amount of direction provided by the inventor/existence of working examples

(i) The compounds within the genus exemplified by the disclosure commensurate in scope to the genus claimed.

(ii)-(iii)No direction or working examples are provided.

The quantity of experimentation needed to make or use the invention

(i) It is not known which of the unrepresented compounds meet the limitations of the claims, namely possession of required activity. It would require undue experimentation for the artisan to first test which of the compounds possess this activity before being able to practice the invention commensurate in scope with the breadth of the instant claims.

(ii)-(iii)The disclosure provides merely a general suggestion of an idea that could be developed into the claimed invention. Based on the disclosure, one of ordinary skill could not make or use the crystalline/amorphous/solvated forms of the

claimed compounds without first making a substantial inventive contribution. Thus, the quantity of experimentation needed to practice the "invention" is undue.

(iii) Prodrug: the disclosure provides merely a general suggestion of an idea that could be developed into the claimed invention. Based on the disclosure, one of ordinary skill could not make or use prodrugs of the claimed compounds without first making a substantial inventive contribution. Thus, the quantity of experimentation needed to practice the "invention" is undue.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claim 1 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Appropriate correction is required for (a) – (c).

(a) Variable R^1 is defined as "lower alkoxy alkyl-O-". It is unclear what structure this substituent entails. For the purpose of examination, this substituent was assumed to be "lower alkoxy".

(b) Variables R^3 and R^4 are defined as "...and oxygen or nitrogen atoms may be inserted in the chain or ring in a chemically stable position". It is unclear what structure this definition entails. For the purpose of examination, this structural definition was taken to mean that R^3 and R^4 could join to form a heterocyclic ring further comprising additional oxygen or nitrogen atoms.

(c) The 10^{th} line on page 5 refers to "one 5 R5". It is unclear what structure this definition entails.

12. Claims 9, 11, 12, 13 and 53 r33ejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which appliacant regards as the invention. The claims refer back to an "undefined" previous claim because the identifying number of the claim they refer to is omitted.

13. Claim 18 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 18 refers to "enantiomeric 5 form"; it is unclear what the number 5 refers to.

14. Claim 19 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 19 is drawn to "complex" of the compound according to claim 1; it is unclear what "complex" refers to.

Allowable Subject Matter

15. The following is a statement of reasons for the indication of allowable subject matter. The elected invention shown in Scheme 1 is novel and non-obvious over the art of record. The closest prior art, which is a protein kinase inhibitor, is Compound#5 from US 7,067,506 (column 27-28). The instant compounds contain the following structural limitation that are not anticipated or made obvious by the prior art: (a) urea moiety is attached to two phenyl rings (prior art compound has urea moiety attached to phenyl and pyrazine); (b) "western" phenyl ring is further attached to phenoxy (prior art compound does not have this substitution).

Conclusion

16. No claims allowed.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sun Jae Y. Loewe whose telephone number is (571) 272-9074. The examiner can normally be reached on M-F 7:30-5:00 Est.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on (571) 272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Sun Jae Y. Loewe, Ph.D.
Technology Center 1600
Art Unit 1609

JANET L. ANDRES
SUPERVISORY PATENT EXAMINER